UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/735,296	01/14/00	WOO	5 A923-054

EXAMINER

HM22/1002

020583
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ART UNIT	PAPER NUMBER
1642	6

DATE MAILED: 10/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/735,296	Applicant(s) Chen et al
	Examiner MINH TAM DAVIS	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 19, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☐ Claim(s) _____ is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-25* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

It is noted that claims 1 and 13-14 are improper implied Markush claims, because different members of the implied Markush groups are structurally and thus patentably distinct. That is 4-1BB ligand, nucleic acid molecules encoding 4-1BB ligand, anti-4-1BB antibodies, and nucleic acid molecules encoding anti-4-1BB antibodies are structurally distinct and thus patentably distinct. Similarly, an IL, nucleic acid molecules encoding said IL, antibodies against said IL, and nucleic acid molecules encoding antibodies against said IL are structurally distinct and thus patentably distinct.

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

Groups 1-60. Claims 1-12 are drawn to a combination of a compound that activates one or more cytokine receptors and a compound that activates one or more co-stimulatory molecules expressed on activated immune cells. It is noted that claim 1 is an improper implied Markush claim, since it is clearly meant to encompass activators that are not only ligands, but also nucleic acid molecules encoding said ligands, antibodies and nucleic acid molecules encoding said antibodies. Further, MPEP 2173.05(h) provides that when the Markush group occurs in a claim reciting a process or a combination it is sufficient if the members of the group are disclosed in the specificaiton to possess at least one property in common which is responsible for their function in the claimed relationship and it is clear from their very nature or from the prior art that

all of them possess this property. The members of the implied Markush groups recited in claim 1 do not share a common property, nor do they function by a common mechanism to augment activated immune cells. Thus claims 1-12 are drawn to four distinct types of activators of cytokine receptors, and four distinct types of activators of co-stimulatory molecules. It is also noted that the number of possible combination of a compound that activates one or more cytokine receptors and a compound that activates one or more co-stimulatory molecules was determined by a factorial calculation, that is 4 factorial for the activator of cytokine receptors or 30 possible combinations, and 4 factorial for the activator of co-stimulatory molecules or 30 possible combinations, for a total of 60 groups. Each of the combination is a separate invention, that is a separate group, and **not a species**, classified in class 530, subclass 350. Applicant is required to elect a single group consisting of a combination of a specific type of activator compound that activates one or more cytokine receptors and a specific type of activator compound that activates one or more co-stimulatory molecules. Further, Applicant is required to identify and claim the number of cytokine receptors and the number of co-stimulatory molecules that are activated, since each combination of more than 1 of each represents a distinct group. Claims 1-12 will be examined as they are drawn to the elected group.

Groups 61-120. Claims 13, 15, 17, 19, 21-25 are drawn to a method of preventing or treating cancer, comprising administering a combination of a compound that activates one or more cytokine receptors and a compound that activates one or more co-stimulatory molecules expressed on activated immune cells. It is noted that claim 13 is an improper implied Markush

claim, since it is clearly meant to encompass methods using activators that are not only ligands, but also nucleic acid molecules encoding said ligands, antibodies and nucleic acid molecules encoding said antibodies. Further, MPEP 2173.05(h) provides that when the Markush group occurs in a claim reciting a process or a combination it is sufficient if the members of the group are disclosed in the specificaiton to possess at least one property in common which is responsible for their function in the claimed relationship and it is clear from their very nature or from the prior art that all of them possess this property. The members of the implied Markush groups recited in claim 13 do not share a common property, nor do they function by a common mechanism to augment activated immune cells. Thus claims 13, 15, 17, 19, 21-25 are drawn to four distinct methods using four distinct types of activators of cytokine receptors, and four distinct methods using four distinct types of activators of co-stimulatory molecules. It is also noted that the number of possible combination of a method using a compound that activates one or more cytokine receptors and a compound that activates one or more co-stimulatory molecules was determined by a factorial calculation, that is 4 factorial for the method using an activator of cytokine receptors or 30 possible combinations, and 4 factorial for the method using an activator of co-stimulatory molecules or 30 possible combinations, for a total of 60 groups. Each of the methods using each combination is a separate invention, that is a separate group, and **not a species**, classified in class 514, subclass 2. Applicant is required to elect a single group consisting of a method using a combination of a specific type of activator compound that activates one or more cytokine receptors and a specific type of compound that activates one or

more co-stimulatory molecules. Further, Applicant is required to identify and claim the number of cytokine receptors and the number of co-stimulatory molecules that are activated, since each combination of more than 1 of each represents a distinct group. Claims 13, 15, 17, 19, 21-25 will be examined as they are drawn to the elected group.

Groups 121-180. Claims 14, 16, 18, 20, 21-25 are drawn to a method of preventing or treating an infectious disease, comprising administering a combination of a compound that activates one or more cytokine receptors and a compound that activates one or more co-stimulatory molecules expressed on activated immune cells. It is noted that claim 14 is an improper implied Markush claim, since it is clearly meant to encompass methods using activators that are not only ligands, but also nucleic acid molecules encoding said ligands, antibodies and nucleic acid molecules encoding said antibodies. Further, MPEP 2173.05(h) provides that when the Markush group occurs in a claim reciting a process or a combination it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is responsible for their function in the claimed relationship and it is clear from their very nature or from the prior art that all of them possess this property. The members of the implied Markush groups recited in claim 14 do not share a common property, nor do they function by a common mechanism to augment activated immune cells. Thus claims 14, 16, 18, 20, 21-25 are drawn to four distinct methods using four distinct types of activators of cytokine receptors, and four distinct methods using four distinct types of activators of co-stimulatory molecules. It is also noted that the number of possible combination of a method using a

compound that activates one or more cytokine receptors and a compound that activates one or more co-stimulatory molecules was determined by a factorial calculation, that is 4 factorial for the method using an activator of cytokine receptors or 30 possible combinations, and 4 factorial for the method using an activator of co-stimulatory molecules or 30 possible combinations, for a total of 60 groups. Each of the methods using each combination is a separate invention, that is a separate group, and **not a species**, classified in class 514, subclass 2. Applicant is required to elect a single group consisting of a method using a combination of a specific type of activator compound that activates one or more cytokine receptors and a specific type of compound that activates one or more co-stimulatory molecules. Further, Applicant is required to identify and claim the number of cytokine receptors and the number of co-stimulatory molecules that are activated, since each combination of more than 1 of each represents a distinct group. Claims 14, 16, 18, 20, 21-25 will be examined as they are drawn to the elected group.

In addition, upon the election of any of groups 1-180, further election of the following patentably distinct species of the claimed invention is required:

Treating or prevention of a disease.

IL-12, IL-15 or IL-18.

Upon the election of any of groups 1-60, further election of the following patentably distinct species of the claimed invention is required:

Cancer or infectious disease.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions (1-60) and (61-180) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. 806.05 (h). In this instant case, a polypeptide could be used for several purposes, e.g. for biochemical assay, for making antibodies, and for making an affinity column to purify its antibodies; a DNA sequence could be used for the detection of similar DNA or RNA sequences, for making an expression vector, and for producing its encoded protein; and an antibody could be used for immunoassay, for purification of its antigen, and for detection of diseases.

The products of groups 1-60 are patentably distinct, because they are drawn to entirely different biochemicals, having different structures.

The methods of groups (61-120) (121-180) are distinct from each other because they differ at least in objectives, dosages, and/or schedules used, response variables and criteria for success.

The methods of groups 61-180) are distinct from each other because they differ at least in method steps, reagents and/or dosages, and/or schedules used, response variables and criteria for success.

The species prevention and treatment are distinct, because a treated disease does not necessarily mean that said disease is prevented.

The species IL-12, IL-15 or IL-18 are distinct because they are structurally distinct.

The species cancer and infectious disease of claims 1-60 are distinct, because they are different disease, with different etiology.

Because these inventions are distinct for the reason given above and have acquired a separate status in the art, and because the searches for the groups are not co-extensive, restriction for examination purposes as indicated is proper.

Applicants are required under 35 USC 121 to elect a single disclosed group for prosecution on the merits to which the claims shall be restricted. Applicant is further advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 USC 103 of the other invention.

Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendement of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. 1.48(b) and by the fee required under 37 C.F.R. 1.17(h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Minh-Tam B. Davis whose telephone number is (703) 305-2008. The examiner can normally be reached on Monday-Friday from 9:30am to 3:30pm, except on Wesnesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0916.

Minh-Tam B. Davis

September 29, 2001

SUSAN UNGAR, PH.D
PRIMARY EXAMINER